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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,071	05/08/2001	Ann Marie Schmidt	0575/55424-Z/JPW/SHS/MVM	3248

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EXAMINER

KAUSHAL, SUMESH

ART UNIT

PAPER NUMBER

1636

14

DATE MAILED: 09/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application N .

09/851,071

Applicant(s)

SCHMIDT ET AL.

Examiner

Sumesh Kaushal Ph.D.

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 July 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 17, 19-21 and 34-36 is/are pending in the application.
- 4a) Of the above claim(s) 22-32 and 36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 17, 19-21 and 34-35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other:  |

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### DETAILED ACTION

Applicant's response filed on 07/17/03 has been acknowledged.

*Claims 18, 33, 37 and 38 are canceled.*

*Claims 17, 21 and 34 are amended.*

*Claims 17, 19-21 and, 34-35 are pending and are examined in this office action.*

This application contains claim 22-32 and 36 drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

*The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.*

► *Applicants are required to follow Amendment Practice under revised 37 CFR §1.121 (<http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm>). Each amendment document that includes a change to an existing claim, or submission of a new claim, **must include a complete listing of all claims** in the application. After each claim number, the status must be indicated in a parenthetical expression, and the text of each claim under examination (with markings to show current changes) must be presented. The listing will serve to replace all prior versions of the claims in the application.*

### ***Claim Rejections - 35 USC § 102***

Claims 17, 19-21 and 34 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Chintala et al (Cancer Lett 103:21-208, 1996), for the same reasons of record as set forth in the office action mailed on 04/10/03.

The invention as claimed is drawn to a method for evaluating the ability of an agent to inhibit tumor cell spreading, wherein the agent inhibits the interaction between tumor cell and an extra cellular matrix molecule.

The cited art teaches a method for evaluating the ability of an agent to inhibit tumor invasion in a tumor cell culture (page 201 abstract). The invasive ability of the SNB19 and U251 human glioma cells in-vitro was measured by the invasion of cells through metrigel in 48-well microchemotaxis chamber (page 203, col.1 para.1; page 204, fig-2; page 205, fig 3, 4; page 207, fig-7). The cited art further teaches the evaluation of candidate agents that inhibit an interaction

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between the tumor cell and an extracellular matrix molecule like collagen, laminin, fibronectin and  $\alpha 3 \beta 1$  integrin (page 201-202; page 204, fig-2; page 205, fig 3, 4, page 207, fig-7). The cited art further teaches that integrins are transmembrane heterodimeric glycoproteins comprised of an  $\alpha(16)$  and  $\beta(8)$  subunits, which can combine to form at least 20 receptor types (page 201-202). In addition cited art teaches RGD inhibits the interaction of glioblastoma cell lines with fibronectin in a dose dependent fashion (page 203, col.2 para.2). Thus the cited art clearly teaches the method for evaluating the ability of an agent to inhibit tumor invasion and a composition comprising the agent identified using the method as claimed.

***Response to arguments***

The applicant argues that Chintala fails to teach each and every limitation of the claimed method. The applicant argues that the cited art fails to teach the step of admixing with cell culture media an effective amount of agent known to inhibit the interaction between tumor cell and extracellular matrix molecule.

However, this is found NOT persuasive because the invasive assay disclosed on page-203 of instant reference clearly anticipates all the elements of the invention as claimed. The invasive assay teaches the treatment of cells with candidate agents, which encompasses the step a) and b) of claim 17. Furthermore the invasive assay determines the spread of tumor cells by counting the cells which passed through the matrigel to the lower side of the filter. This clearly anticipate the step c) of claim 17. The cited art teaches the comparative evaluation of BSA, Coll IV, Fibronectin and Laminin in cell migration, which clearly anticipate the step b) of claim 1. In addition cited art teaches RGD inhibits the interaction of glioblastoma cell lines with fibronectin in a dose dependent fashion (page 203, col.2). Thus given the broadest reasonable interpretation the Invasive Assay as taught by the cited art clearly anticipate all elements of the claimed invention.

Claims 17, 19-21 and 34-35 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Softer et al (PNAS 89:1557-1561, 1992), for the same reasons of record as set forth in the office action mailed on 04/10/03.

The invention as claimed is drawn to a method for evaluating the ability of an agent to inhibit tumor cell spreading, wherein the agent inhibits the interaction between tumor cell and an extra cellular matrix molecule. The scope of candidate agent encompasses a molecule, which inhibits the interaction of tumor cell with an extra cellular matrix, wherein the extracellular matrix is an  $\alpha V\beta 3$ ,  $\alpha V\beta V$  or  $\alpha I\beta II$  integrin.

The cited art teaches a method for evaluating the ability of an agent to inhibit tumor invasion using an in-vitro invasion assay in context with  $\alpha V\beta 3$  integrin (page 1557 abstract). The cited art explored the relationship between the function and expression of  $\alpha V\beta 3$  integrin in A375M human melanoma cells and ability of these cells to invade in-vitro by modulating  $\alpha V\beta 3$  integrin with either antibodies or its ligand vitronectin (page 1557 col.2 para.1). The cited art teaches that in-vitro invasion assay, wherein in the assay was performed in membrane invasion culture system (MICS) using polycarbonate filter containing 10 $\mu$ m pores coated with Matrigel. The cited art further teaches the determination of invasion potential of the treated and untreated tumor cells (page 1558, col.1 para.2, page 1559, fig-3). The cited art teaches that pretreatment of tumor cells with soluble vitronectin prior to assay resulted in increase in tumor cell invasion (page 1559, col.2 para.2). The cited art further teaches the A375M human melanoma cells express the  $\alpha V\beta 3$  integrin, wherein the  $\alpha V\beta 3$  integrin play an active role in mediating the attachment of these cells to their substratum. The cited art further teaches that  $\alpha V\beta 3$  integrin is known to bind to number of Arg-Gly-Asp (RGD) containing proteins such as vitronectin, laminin and entacti/nidogen (page 1559, col.2 para.5). Thus the cited art clearly teaches the method for evaluating the ability of an agent to inhibit tumor invasion and a composition comprising the agent identified using the method as claimed.

#### ***Response to arguments***

The applicant argues that Softer fails to teach each and every limitation of the claimed method. The applicant argues that the cited art fails to teach the step of admixing with cell culture media an effective amount of agent known to inhibit the interaction between tumor cell and extracellular matrix molecule.

However, this is found NOT persuasive because the cited art clearly teaches an in-vitro invasion assay system, wherein in the assay was performed in membrane invasion culture system

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(MICS) using polycarbonate filter containing 10um pores coated with Matrigel. The cited art further teaches the determination of invasion potential of the treated and untreated tumor cells (page 1558, col.1 para.2, page 1559, fig-3). Figure-3 clearly teaches the evaluation of invasiveness of A375M melanoma cells with or without treatment with anti-integrin antibody ( $\alpha V\beta 3$  integrin). The cited art further teaches the inoculation of fresh antibody daily throughout the course of 72-hr assay. Therefore the invasion assay as taught by the cited art clearly anticipate the invention as claimed.

### ***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 703-305-6838. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9306 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

***S. Kaushal***

PATENT EXAMINER

  
**JEFFREY FREDMAN  
PRIMARY EXAMINER**